REMARKS

The Office Action of July 1, 2004 has been carefully considered and the following response prepared. Claims 6, 9-11, 15-23, 25, 26, 31-59, 61, 62, 65, 70, 71, 75 and 77-80 are pending in the application. Claims 10, 11, 15, 16, 21, 22 and 31-59 have been withdrawn from consideration. Claims 71 and 78-80 have been amended. Claims 61, 62 and 70 have been canceled without prejudice.

At page 2 of the Office Action, the Examiner rejected claims 6, 17-20, 23, 25-26, 61-62, 65, 70-71 and 78-80 under 35 USC 112, first paragraph as not enabled. The basis for the rejection is that the specification, while being enabling for methods of increasing the production of cysteine, glutathione, methioning and sulfur derivatives in a plant by transformation with a gene encoding an Arabidopsis cysteine-insensitive SATase, is not enabling for methods using a gene encoding any cysteine-insensitive SATase. Additionally, the Examiner indicated that, while transit peptides in general are broadly enabled, transit peptides comprising a plant transit peptide, an N-terminal portion of a mature plastid protein linked by its N-terminus to the C-terminus of the plastid transit peptide, and a second plastid transit peptide linked by its N-terminus to the C-terminus of the N-terminal portion of a mature plastid protein are not broadly enabled because the only such transit peptide taught in the specification is OTP.

Applicants again traverse this rejection. While Applicants disagree with the Examiner's characterization of the claims as not enabled, solely in order to advance prosecution, the claims have been amended to have the scope indicated as enabled by the Examiner. Independent claims 78-80 have been amended to state that the cysteine-insensitive serine acetyl transferase is an *Arabidopsis thaliana* cysteine-insensitive serine acetyl transferase. Claims 61 and 62 have been canceled without prejudice. Claim 70 has been canceled without prejudice. Claim 71 has been amended to change its dependency from canceled claim 70 to claim 25 (from which canceled claim 70 depended). Withdrawal of this section 112, first paragraph rejection is requested.

At page 5 of the Office Action, the Examiner rejected claims 6, 17-20, 23, 25-26, 61-62, 65, 70-71 and 78-80 under 35 USC 112, as failing to comply with the written description requirement. The rationale for this rejection is that the specification does not provide written

description of the invention within the full-scope of the claims because it does not provide written description of a representative number of cysteine-insensitive SATs from plants and bacteria. Additionally, the Examiner stated that the specification does not provide a written description of the full-scope of the claimed transit peptides comprising the N-terminal portion of any mature plastid protein linked by its-N-terminus to the C-terminus of any plastid transit peptide, and any second plastid transit peptide linked by its N-terminus to the C-terminus of the N-terminal portion of a mature plastid protein, except for the transit peptide OTP.

Applicants traverse this rejection. Again, although Applicants disagree with the Examiner's characterization of the claims as failing to satisfy the written description requirement of section 112, first paragraph, solely in order to advance prosecution, the claims have been amended to have the scope indicated as adequately described by the Examiner. Independent claims 78-80 have been amended to state that the cysteine-insensitive serine acetyl transferase is an *Arabidopsis thaliana* cysteine-insensitive serine acetyl transferase. Claims 61 and 62 have been canceled without prejudice. Claim 70 has been canceled without prejudice. Claim 71 has been amended to change its dependency from canceled claim 70 to claim 25 (from which canceled claim 70 depended). Withdrawal of this section 112, first paragraph rejection is requested.

At page 7 of the Office Action, the Examiner rejected claims 75, 77 and 79-80 under 35 USC 103 as being unpatentable over Saito *et al.*, Plant Physiol. 106: 887-895, 1994, in view of each of Noji *et al.*, J. Biol. Chem. 273: 32739-32745, 1998 and Ruffet *et al.*, Eur. J. Biochem 227: 500-509, 1995. The Examiner stated that it would have been obvious to one of ordinary skill in the art to modify the method of increasing the production of cysteine in a plant by overexpressing a cytoplasmic cysteine synthase in a plant as taught by Saito *et al.* and to use a nucleic acid encoding another enzyme required for cysteine biosynthesis, SATase, as described in each of Noji *et al* and Ruffet *et al.*, because SATase has a role in the regulation of cysteine biosynthesis as disclosed in Noji *et al.* and because Saito *et al.* suggest expressing SATase in the plants for maximal cysteine formation.

Applicants traverse this rejection. Saito *et al.*, Noji *et al.* and Ruffet *et al.* were discussed

previously in Applicants response to the Office Action of April 29, 2003.

As discussed in Applicants' previous response, it is well-established that before a conclusion of obviousness may be made based on a combination of references, there must be a reason, suggestion or motivation in the prior art to lead an inventor to combine those references. Saito *et al.* discloses experiments using a different enzyme, cysteine synthase. At best, Saito *et al.* arguably suggests overexpression of both cysteine synthase and SAT. Noji *et al.* and Ruffet *et al.* do not cure the deficiencies of Saito *et al.* Noji *et al.* discloses experiments of feedback regulation and subcellular localization of SAT, but does not suggest that culturing plant cells transformed with a nucleic acid sequence encoding an *Arabidopsis* cysteine-insensitive serine acetyltransferase could increase production of cysteine. Ruffet *et al.* discloses experiments on the subcellular distribution of SAT from *Pisum sativum* and isolation and characterization of a cytosolic isoform of SAT from *A. thaliana* referred to as SAT5, but there is no suggestion in Ruffett *et al.* that cysteine production in plants could be increased by overexpressing SAT. There is thus no suggestion, reason or motivation in the cited prior art to overexpress SAT alone to increase production of cysteine, glutathione, methionine or sulfur-containing derivatives of methionine by plant cells and plants.

Even assuming *arguendo* that the combination of references is proper, the combined disclosures of the references are insufficient to support the Examiner's conclusion that the claimed methods of increasing the production of cysteine are obvious. The combined disclosures of Saito *et al.*, Noji *et al.* and Ruffet *et al.* still fail to suggest that cysteine production could be increased by overexpressing SAT alone in plant cells or plants as claimed. The combined disclosures of Saito *et al.*, Noji *et al.* and Ruffet *et al.* at best suggest that overexpression of both cysteine synthase and SAT are necessary to obtain increased production of cysteine and glutathione, even if such an increase would be possible. Applicants' claimed methods are not obvious over Saito *et al.* in view of Noji *et al.* and Ruffet *et al.*.

Claim 79 is drawn to a method for increasing the production of cysteine, glutathione, methionine or sulfur-containing derivatives of methionine by plant cells, the method consisting of culturing plant cells transformed with a nucleic acid sequence encoding an *Arabidopsis*

thaliana cysteine-insensitive serine acetyltransferase; whereby the transformed plant cells overexpress serine acetyltransferase resulting in an increase in production of cysteine, glutathione, methionine, or sulfur-containing derivatives of methionine by the transformed plant cells in comparison with the level observed in nontransformed plant cells of the same type as the transformed plant cells. Similarly, claim 80 is directed to a method for increasing the production of cysteine, glutathione, methionine or sulfur-containing derivatives of methionine by a plant, the method consisting of culturing plant cells transformed with a nucleic acid sequence encoding an *Arabidopsis thaliana* cysteine-insensitive serine acetyltransferase; and regenerating a transformed plant from said transformed plant cells, whereby the transformed plant overexpresses serine acetyltransferase resulting in an increase in production of cysteine, glutathione, methionine, or sulfur-containing derivatives of methionine by the transformed plant in comparison with the level observed in a nontransformed plant of the same type as the transformed plant.

In the Office Action mailed December 19, 2003 (page 2, paragraph 5), the Examiner withdrew a rejection under 35 USC 103 of independent claim 60 (now canceled) in view of the same combination of references, on the basis of Applicants' amendments to limit the method to one consisting of overexpressing serine acetyltransferase. Claim 60 was canceled and rewritten as claim 78 for reasons unrelated to the rejection under section 103. Canceled claim 60 is set out below:

> 60. (canceled) A method for increasing the production of cysteine, glutathione, methionine or sulfur-containing derivatives of methionine by plant cells and plants in comparison with the level observed in nontransformed plant cells and plants, said method consisting of overexpressing serine acetyltransferase in plant cells or in plants containing said plant cells transformed with a nucleic acid sequence encoding a cysteine-insensitive serine acetyltransferase, whereby overexpression of serine acetyltransferase results in the increased production of cysteine, methionine, glutathione, methionine or sulfur-containing derivatives of methionine in comparison with the level observed in nontransformed plant cells .

The methods of claim 79 and 80 differ from claim 60 by reciting "culturing" plant cells

transformed with a nucleic acid sequence encoding an *Arabidopsis thaliana* cysteine-insensitive serine acetyltransferase rather than "overexpressing" serine acetyltransferase in plant cells or in plants containing said plant cells transformed with a nucleic acid sequence encoding a cysteine-insensitive serine acetyltransferase. As in claim 60, the transformed plant cells or transformed plants containing such transformed plant cells recited in claims 79 and 80 are transformed with SAT and overexpress SAT alone, whereby overexpression of serine acetyltransferase results in the increased production of cysteine, methionine, glutathione, methionine or sulfur-containing derivatives of methionine in comparison with the level observed in nontransformed plant cells. The present rejection of claims 79 and 80, and dependent claims 75 and 77, should be withdrawn for the same reason, because these claims are also limited to a method wherein SAT alone is overexpressed.

Withdrawal of this section 103 rejection is requested.

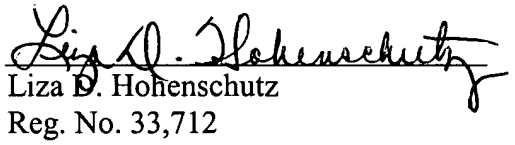
In view of the above, the present application is believed to be in a condition ready for allowance. Entry of the amendments to claims 71 and 78-80 are requested as these amendments place the claims in condition for allowance or at least better form for appeal. Reconsideration of the application is requested and an early Notice of Allowance is earnestly solicited.

No fee is believed to be due. Please charge any fees that may be associated with the filing of this response to Deposit Account 03-2775.

Respectfully submitted,

CONNOLLY BOVE LODGE & HUTZ LLP

Date: October 1, 2004

By: 

Liza D. Hohenschutz
Reg. No. 33,712
P.O. Box 2207
Wilmington, Delaware 19899
(302) 888-6420
Attorney for Applicants

LDH/alh/